

of ordinary skill in the art to treat cancer with a combination of 4-desacetyl-4-methylcarbonate taxol, which is a taxane derivative, and doxorubicin in view of the method in Bissery, which discloses the use of paclitaxel, taxotere and their derivatives.

This rejection is respectfully traversed on the grounds that the Examiner has failed to establish a prima facie case of obviousness.

The Examiner states at page 3 of the Office Action that, "use of a known member of a class of materials in a process is not patentable if other members of the class were known to be useful for that purpose, even though the results are better than expected." Applicants respectfully submit that this statement is erroneous and contrary to the current state of the law. Specifically, the Examiner's statement ignores the fact that more evidence is required to establish a prima facie case of obviousness and that even when a proper prima facie of obviousness is established it may be rebutted by evidence, such as unexpected results. However, even if the Examiner's statement of the law was correct, the specific structure of the present claims, 4-desacetyl-4-methylcarbonate taxol, is neither disclosed, taught, or suggested by Bissery.

Where a particular species found in a reference is included in a claimed genus, that species is said to anticipate the genus. See MPEP §2131.02. However, there is no such species in Bissery that would anticipate the taxane derivative of the present claims. Therefore, the only question remaining is whether the specific structures of Bissery, specifically paclitaxel and taxotere, render the present claims obvious. This analysis should be conducted using the "Genus-Species Guidelines" present in MPEP §2144.

Whether a particular species or a subgenus is obvious in view of a prior art genus that is disclosed in a single reference depends on several factors. A genus alone will not anticipate an individual species or subgenus. The MPEP provides "Genus-Species Guidelines" in Section 2144 to determine whether a Section 103 rejection is appropriate. The guidelines apply to both a species as well as to a subgenus. "The claimed invention may not be dissected into discrete

elements to be analyzed in isolation, but must be considered as a whole.” As required for all Section 103 references, there still must be some teaching or suggestion within the prior art reference to motivate one to prepare the claimed species or subgenus in order to render the species or subgenus obvious. Factors that can contribute to this analysis include:

- (a) the size of the genus;
- (b) the express teachings of the reference;
- (c) any teachings of structural similarity;
- (d) any teachings of similar properties or uses;
- (e) the predictability of the technology; and
- (f) any other teaching to support the selection of the species or subgenus.

The Examiner states that Bissery teaches antitumor compositions comprising taxol derivatives in combination with an antibiotic which may include doxorubicin. This alone is not sufficient to establish a case of prima facie obviousness.

Bissery discloses the use of paclitaxel and taxotere including “derivatives of paclitaxel and taxotere,” but there is no disclosure, teaching or suggestion as to how paclitaxel or taxotere may be modified to achieve such a derivative. Assuming, *arguendo*, that Bissery is referring to all derivatives of the taxane moiety, this is an infinite genus. Bissery includes no disclosure, teaching or suggestion to prepare 4-desacetyl-4-methylcarbonate taxol.

The Examiner is only left to rely on a finding of structural similarity between either paclitaxel or taxotere and the taxane derivative, 4-desacetyl-4-methylcarbonate taxol, of the present claims. However, a finding of structural similarity between a prior art compound and a claimed compound is only sufficient to establish a prima facie case of obviousness in limited circumstances. In re Jones 21 USPQ2d 1941, 1943 (Fed. Cir. 1992). These circumstances are limited to instances where the allegedly similar compounds are tri-orthoesters and tetra-orthoesters, stereoisomers, adjacent homologs and structural isomers, or acid and ethyl esters.

Id. None of these situations is applicable as a comparison of the structures of Bissery and that of the present invention.

The Federal Circuit has clearly stated that "generalization is to be avoided insofar as specific structures are alleged to be prima facie obvious one from the other." In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992) *citing* In re Grabiak 226 USPQ 870, 872 (Fed. Cir. 1985). The standard for finding one structure prima facie obvious in view of a similar structure is the same as the standard all obviousness rejections, i.e. there must be some motivation in the reference or a combination of references to prepare the compositions and methods of the present claims. *See* Grabiak and Jones. In other words, "The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound." Jones *citing* In re Lalu, 223 USPQ 1257, 1258 (Fed. Cir. 1984).

Bissery discloses only two compounds, paclitaxel and taxotere and their derivatives. However, Bissery provides no motivation to modify either paclitaxel or taxotere, no any teaching or suggestion as to what modifications may be made to these structures to arrive at a "derivative." Clearly there is no teaching or suggestion in Bissery of 4-desacetyl-4-methylcarbonate taxol.

Bissery fails to support a finding of prima facie obviousness because not only is the genus disclosed by Bissery infinitely large, but also, Bissery provides no motivation, teaching or suggestion to modify the structures of taxotere or paclitaxel. Therefore, reconsideration and withdrawal of the rejections under Section 103 are appropriate and respectfully requested.

As stated above, even if the Examiner had established a prima facie obviousness, the burden would then shift to the Applicant to provide secondary evidence of patentability, which may include unexpected results.


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The compositions and methods of the present invention include a specific taxane derivative in combination with doxorubicin to provide a cancer treatment with a notable reduction in toxicity. Bissery recognizes that toxicity is a problem and suggests that it may be corrected by combining the treatment with the administration of a haematopoietic growth factor. Bissery, column 1, lines 49-54. There is no teaching or suggestion that any particular taxane derivative may, in combination with doxorubicin, provide a decrease toxicity. In fact, Bissery seeks to use the least effective dosage of the doxorubicin and paclitaxel or taxotere by taking advantage of the synergistic effect of the combination of doxorubicin with either paclitaxel or taxotere. Column 2, lines 1-4 and 25-30.

By contrast to Bissery, the combination of 4-desacetyl-4-methylcarbonate taxol with doxorubicin, is alone sufficient to achieve a decrease in toxicity. The advantage of this combination is clear considering that in general higher dosage of the treatment provides a greater biological activity.

Applicants respectfully submit that the application is in condition for allowance and favorable action is therefore solicited. Should the Examiner have any questions, the undersigned will be pleased to address them by telephone.

Respectfully submitted,



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